

AMENDMENT

In the Specification

Please replace the sequence listing with the listing attached as Appendix A of this response.

On page 20, lines 3-14, please replace the paragraph with the following:

FIG. 6A shows a presentation of nucleic acid sequences comprising *attB* and *attH*, respectively (SEQ ID NO:[21]26 and SEQ ID NO:[22]27). FIG. 6B shows a representation of partial sequences of *attP* and *attP** (SEQ ID NO:[23]28 and SEQ ID NO:[24]29). (A): Sequence comparison between *attB* and *attH*. The Int core binding sites B and B' in *attB* are marked with a dash in top of the sequences. The Int core binding sites H and H' in *attH* are marked with a dashed line in top of the sequences. The overlap sequences are characterized by open rectangles. Differences in the sequences are marked with a perpendicular double dashes. The numbering of the residues in the core and overlap regions relate to the center of the overlap designated with O and defined by Landy and Ross ((1977), Science, 197, pp.1147). The sequence from -9 to +11 is the *attB* and *attH* site, respectively. (B): Sequence comparison between the partial sequences of *attP* and *attP**, corresponding to *attB* and *attH*, respectively. The designations are used as in FIG. 6A.

On page 21, line 23 to page 22, line 4, please replace with the following:

The eukaryotic expression vectors for wild-type Int (pKEXInt), Int-h (pKEXInt-h), Int-h/218 (pKEXInt-h/218) and pEL13 are derivatives of pKEX-2-XR (Rittner et al. (1991), Methods Mol. Cell. Biol., 2, pp. 176). Said vector includes the human cytomegalo virus promotor/enhancer element (CMV) and the RNA splicing and polyadenylation signal elements of the small simian virus 40 (SV40) tumor antigen. The Int genes were cloned by PCR with the following primers:

(3343) 5'-GCTCTAGACCACCATGGGAAGAAGGCGAAGTCA-3' (SEQ ID NO:[1]6), located at the 5' end of the Int gene and (3289) 5'-AAGGAAAGCGGCCGCTCATTATTTGATTTCATTTTGTCC-3' (SEQ ID NO:[2]7), located at the 3' end.

On page 22, lines 15-21, please replace with the following paragraph:

Starting from *attP attP** was constructed by PCR mutagenesis. The following oligonucleotides were used:

(O3) 5'-G TTCAGCTTTT TGATACTAAGTTG-3' (SEQ ID NO:[3]8),
(O4) 5'-CAACTTAGTATCAAAAAGCTGAAC-3' (SEQ ID NO:[4]9),
(PC) 5'-TTGATAGCTCTTCCGCTTTCTGTTACAGGTCACCTAATACC-3' (SEQ ID NO:[5]10) and
(PD) 5'-ACGGTTGCTCTTCCAGCCAGGGAGTGGGACAAAATTGA-3' (SEQ ID NO:[6]11).

On page 23, lines 1-9, please replace with the following:

The substrate vectors are derivatives of pEGFP (Clontech). The recombination cassettes are under the control of the CMV promoter, guaranteeing a strong constitutive expression. pGFP*attB/attP* was constructed by cutting the GFP gene (green fluorescence protein) out of pEGFP by AgeI and BamHI first. The wild-type *attB* sequence was inserted as double stranded oligonucleotide into the vector cleaved with AgeI using the following oligonucleotides:

(B10B) 5'-CCGGTTGAAGCCTGCTTTTTTATACTAACTTGAGCGAACGC-3 (SEQ ID NO:[7]12) and

(BOB1) 5'-AATTGCGTTCGCTCAAGTTAGTATAAAAAAGCAGGCTTCAA-3' (SEQ ID NO: [\[\[8\]\]13](#)).

On page 23, lines 11-15, please replace with the following:

The wild-type *attP* sequence was amplified by PCR from the vector pAB3 (Dröge, P. and Cozzarelli, N. (1989) Proc. Natl. Acad. Sci., **86**, pp. 6062) using the following primers:

(p7) 5'-TCCCCCGGGAGGGAGTGGGACAAAATTGA-3' (SEQ ID NO: [\[\[9\]\]14](#)) and
(p6) 5'-GGGGATCCTCTGTTACAGGTCACATAATAC-3' (SEQ ID NO: [\[\[10\]\]15](#)).

On page 23, line 27 to page 24, line 5, please replace with the following:

With the exception of the recombination sequences, pGFP*attL/attR* is identical to pGFP*attB/attP*. The vector was constructed by first recombining pGFP*attB/attP* in *E. coli* leading to the formation of *attL* and *attR*. The subsequently with regard to the CMV promotor correctly orientated GFP gene was excised with a partial restriction reaction with BsiEI and HindIII. The GFP gene was first of all amplified by PCR using the following primers to insert it in inverted orientation with regard to the CMV promotor:

(p2) 5'-AATCCGCGGTCGGAGCTCGAGATCTGAGTCC-3' (SEQ ID NO: [\[\[11\]\]16](#)) and
(p3) 5'-AATCCCAAGCTTCCACCATGGTGAGCAAGGG-3' (SEQ ID NO: [\[\[12\]\]17](#))
(FIG. 3).

On page 24, lines 15-19, please replace with the following:

The human *attB* homologue, *attH*, was amplified from purified human DNA by PCR using the following primers:

(B3) 5'-GCTCTAGATTAGCAGAAATTCTTTTTG-3' (SEQ ID NO:[13]18) and
(B2) 5'-AACTGCAGTAAAAAGCATGCTCATCACCCC-3' (SEQ ID NO:[14]19).

On page 26, lines 14-21, please replace with the following:

To prove intramolecular, integrative and excisive recombination 0.4 µg genomic DNA was amplified by PCR using 20 to 50 pmol of the following primers:

(p1) 5'-GGCAAACCGGTTGAAGCCTGCTTTT-3' (SEQ ID NO:[15]20);
(p2) 5'-AATCCGCGGTCGGAGCTCGAGATCTGAGTCC-3' (SEQ ID NO:[11]16);
(p3) 5'-AATCCCAAGCTTCCACCATGGTGAGCAAGGG-3' (SEQ ID NO:[12]17);
(p4) 5'-AACCTCTACAAATGTGGTATGG-3' (SEQ ID NO:[16]21),
(p5) 5'-TACCATGGTGATGCGGTTTTG-3' (SEQ ID NO:[17]22);
(p6) 5'-GGGGATCCTCTGTTACAGGTCACCTAATAC (SEQ ID NO:[10]15);
(p7) 5'-TCCCCCGGGAGGGAGTGGGACAAAATTGA-3' (SEQ ID NO:[9]14).

On page 26, line 26 to page 27, line 4, please replace with the following:

Intermolecular integrative recombination of pEL13 was detected as follows. About 400 ng of the genomic DNA of surviving cell populations was incubated with the following oligonucleotides as PCR primers:

(attx1) 5'-AGTAGGAATTCAGTTGATTCATAGTGACTGC-3' (SEQ ID NO:[18]23) and
(B2) 5'-AACTGCAGTAAAAAGCATGCTCATCACCCC-3' (SEQ ID NO:[14]19).

Beginning on page 27, line 8-15, please replace with the following:

The reverse transcriptase PCR (RT-PCR) was carried out with 4 µg isolated RNA. First, the cDNAs were synthesized using oligo-dT primers according to the instructions of the manufacturer (First Strand Synthesis Kit, Pharmacia). Second, a quarter of said cDNAs was used as a template for the subsequent PCR using primers p3 and p4. To test for deletion instead of inversion isolated genomic DNA was amplified with the primers p5 and p6. Beta actin transcripts were analyzed starting from said cDNAs using the primers

(AS) 5'-TAAAACGCAGCTCAGTAACAGTCCG-3' (SEQ ID NO:[19]24) and

(S) 5'-TGGAATCCTGTGGCATCCATGAAAC-3' (SEQ ID NO:[20]25).